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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/512,926	02/25/2000	Fred S. Lamb	P-1057	6913

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EXAMINER	
KIM, JENNIFER M	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/512,926	LAMB, FRED S.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-11,23 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-11,23 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 11, 2004 has been entered.

Claims 1, 6-11 and 23 of record rejected under 35 U.S.C. 103 (a) over Grainger et al. of record is maintained for the reasons stated in the previous office action.

Applicant's newly added claim 25 necessitated the rejection presented in below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The agonist "serotonin" lack literal support in the specification as filed. This is a new matter rejection.

1. Claims 1,6-11 and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific "vasoconstrictor agonist", does not reasonably provide enablement for the term "a vasoconstrictor agonist". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

2. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: All of the rejected claims are drawn to a method to normalize the contractile response of an endothelially-compromised vascular smooth muscle cell in response to a vasoconstrictor agonist in a patient in need of such normalization comprising administering a CLC3 blocker. The nature of

the invention is extremely complex in that it encompasses in response to any vasoconstrictor agonist such that the subject treated with above compounds normalize the contractile response of endothelially-compromised vascular smooth muscle in response to a vasoconstrictor agonist.

Breath of the Claims: The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass normalizing the contractile response of an endothelially-compromised vascular smooth muscle cell in response to **a vasoconstrictor** agonist (many different vasoconstrictor with different chemical structures) in a patient in need of such normalization comprising administering a CLC3 blocker. Each of the vasoconstrictor may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually normalize a response to a vasoconstrictor agonist is minimal. All of the guidance provided by the specification is directed towards specific vasoconstrictor rather than a vasoconstrictor.

Working Examples: All of the working examples provided by the specification are directed toward the specific vasoconstrictor rather than **a vasoconstrictor**.

State of the Art: While the state of the art is relatively high with regard to normalizing in response to the specific vasoconstrictor agonist, the state of the art with regard to a vasoconstrictor is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound

similar to the claimed compounds was administered to a subject to normalize the response to any vasoconstrictor.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual utilization of any vasoconstrictor in a subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of normalizing in response to a vasoconstrictor agonist.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for normalizing in response to a vasoconstrictor agonist. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard to normalizing in response to a vasoconstrictor agonist with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding normalizing in response to a vasoconstrictor agonist with any compound, the entire, unpredictable process would have to be repeated until

successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to normalizing in response to a vasoconstrictor agonist a subject by administration of one of the claimed compounds.

Therefore, a method to normalize the contractile response of an endothelially-compromised vascular smooth muscle cell in response to **a vasoconstrictor agonist** in a patient in need of such normalization comprising administering a CLC3 blocker is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Stromberg (U.S.Patent No. 5,470,883) evidenced by Kifor et al. (U.S.Patent No. 5,658,936).

Stromberg teaches a method of modifying, blocking or reversing the effect of a peripheral vasoconstrictive agents comprising administering a pharmacologically acceptable dose of tamoxifen. (abstract, column 1, lines 45-65). Stromberg teaches the method comprises inhibiting or reversing the peripheral vasoconstrictive effect of agents such as epinephrine, **norepinephrine** or dopamine. (column 2, lines 1-5). Stromberg teaches that tamoxifen inhibits or reverses the peripheral vasoconstrictive

effect to restore blood flow and protect the peripheral tissues to patient intentionally or unintentionally administered vasoconstrictive agents. (column 2, lines 6-16). Stromberg teaches that it is well known in the practice of medicine that norepinephrine is potent vasoconstrictors and extreme caution is used when administered to body parts such as the penis. Stromberg teaches injection of norepinephrine in body part including the penis can lead to vasoconstriction loss of blood flow and tissue necrosis there fore it would be advantageous to provide a method of blocking or reversing the vasoconstrictive effect of a potent vasoconstrictor by administration of an antiestrogenic steroid such as tamoxifen. (column 1, particularly, lines 12-26, abstract).

Kifor et al. report that modulation of penis blood flow causes increase contractility of smooth muscle within the penis. (column 1, lines 14-23).

Applicant's recitation in claim 25 of "an endothelially-compromised vascular smooth muscle cell" in response to a vasoconstrictor agonist in a patient is inherent upon injection of NE in peripheral tissue (i.e. penis) as evidence by Kifor et al. that contraction of vascular smooth muscle of penis is associated with the modulation of blood flow. It is noted that a mechanism by which the active ingredient gives the pharmacological effect does not alter the fact that the compound has been previously used to obtain the same pharmacological effects which would result from the claimed method. The patient, condition to be treated and the effect are the same. An explanation of why that effect occurs does not make the mechanism novel the treatment of the conditions encompassed by the claim. In this instant case, the it is inherent that upon administration of tamoxifen in Stomberg's patients intentionally or unintentionally

administered with NE in peripheral tissue (e.g. penis) would normalize (reverse, inhibit) the contractile response of endothelially-compromised vascular smooth muscle cell in response to the NE.

Response to Arguments

Applicant's arguments filed February 11, 2004 have been fully considered but they are not persuasive. Applicant argues essentially that claim 1 directed to a method to normalize the contractile response of an endothelially-compromized vascular smooth muscle cell to a least one vasoconstrictor agonist in a patient in need of such normalization, comprising administering a effective amount of a CLC3 blocker. This is not persuasive because Grainger et al. disclose that the therapeutic agent (i.e. tamoxifen) can inhibit the activity of the VSMC such as contraction. This disclosure of "inhibiting contraction" encompasses the "normalization" since the effect of inhibition of contraction of VSMC would "normalize" the VSMC. Further, in response to the limitation of "at least one vasoconstrictor agonist", it is obvious that the contraction taught by Gringer et al. had to be resulted from **a vasoconstrictor agent** including physiologic regulators in order to have a contraction effect. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

Jmk
March 19, 2004